IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

Dumas et al.		Confirmation No.:	4965
Serial No.:	10/788, 426	Examiner:	Robinson, Binta M.
Filed:	March 1, 2004	Group Art Unit:	1625

Title: NOVEL BICYCLIC UREA DERIVATIVES USEFUL IN THE TREATMENT OF CANCER AND OTHER DISORDERS

BRIEF ON APPEAL

Mail Stop Appeal Brief
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Further to the Notice of Appeal filed on September 14 2009, please consider Appellants Brief on Appeal.

The fee of $540.00 as set forth under § 41.20(b)(2) is submitted herewith. The Commissioner is hereby authorized to charge any additional fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

(i) REAL PARTY IN INTEREST

The present application is assigned to: Bayer HealthCare LLC, by means of an assignment recorded on November 26, 2008, on reel 021893 at frames 0640-0723.

(ii) RELATED APPEALS AND INTERFERENCES

There are no pending appeals or interferences on subject matter directly related to this application.

(iii) STATUS OF CLAIMS

Claims 1-13 and 24-30 are pending in the present application.

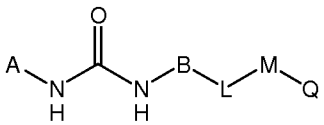
Claims 1-13 and 24-30 are on appeal.

(iv) STATUS OF AMENDMENTS

An amendment after final canceling claims 15-17 and 22 has been filed with this brief on appeal.

(v) SUMMARY OF CLAIMED SUBJECT MATTER

The invention includes ureas of formula (I)



The moiety "A" is a bicyclic heterocycle selected from a defined group. See Appellants specification page 10, line 13 through page 11, line 4. These bicyclic heterocycles are optionally substituted with 1-4 substituents which are independently R^1, OR^1, $S(O)_pR^1$, $C(O)R^1$, $C(O)OR^1$, $C(O)NR^1R^2$, halogen, oxo, cyano, or nitro. See Appellants specification page 13, lines 1-3. The variable p is 0, 1, or 2. See Appellants specification page 15, line 11.

The moiety "B" is phenyl, naphthyl or pyridyl and is optionally substituted with 1-4 substituents which are independently C_1-C_5 linear or branched alkyl, C_1-C_5 linear or branched haloalkyl, C_1-C_3 alkoxy, hydroxy, amino, C_1-C_3 alkylamino, C_1-C_6 dialkylamino, carboxyamide, halogen, cyano, nitro or $S(O)_pR^7$. See Appellants specification page 13, lines 8-11.

The moiety "L" is a single bond or a bridging group which is $-(CH_2)_m-O-(CH_2)_l-$, $-(CH_2)_m-(CH_2)_l-$, $-(CH_2)_m-C(O)-(CH_2)_l-$, $-(CH_2)_m-NR^3-(CH_2)_l-$, $-(CH_2)_m-NR^3C(O)-(CH_2)_l-$, $-(CH_2)_m-S-(CH_2)_l-$ or $-(CH_2)_m-C(O)NR^3-(CH_2)_l-$, where m and l = 0-4. See Appellants specification page 13, lines 18-29.

The moiety "M" is a pyridine ring, optionally substituted with 1-3 substituents which are independently C_1-C_5 linear or branched alkyl, C_1-C_5 linear or branched haloalkyl, C_1-C_3 alkoxy, hydroxy, amino, C_1-C_3 alkylamino, C_1-C_6 dialkylamino, halogen, or nitro. See Appellants specification page 14 lines 1-4.

The moiety Q is $C(O)R^4$, $C(O)OR^4$ or $C(O)NR^4R^5$ where each of R^1, R^2, R^3, R^4 and R^5 is independently, hydrogen, C_1-C_5 linear, branched, or cyclic alkyl, phenyl, C_1-C_3 alkyl-phenyl, up to per–halo substituted C_1-C_5 linear or branched alkyl,

$-(CH_2)_q-X$, wherein X is a 5 or 6 membered heterocyclic ring, containing at least one atom selected from oxygen, nitrogen and sulfur, which is saturated, partially saturated, or aromatic, or a 8-10 membered bicyclic heteroaryl having 1-4 heteroatoms which are O, N or S, or

$-(CH_2)_q-Y$, where Y is $C(O)R^6$, $C(O)OR^6$ and $C(O)NR^6R^7$, where $R^6 - R^7$ are independently hydrogen, C_1-C_5 linear, branched, or cyclic alkyl, phenyl, C_1-C_3 alkyl-phenyl, or up to per–halo substituted C_1-C_5 linear or branched alkyl. See Appellants specification page 14, lines 6-19. Each of R^1, R^2, R^3, R^4, R^5, R^6 and R^7 is optionally substituted. See Appellants specification page 15, lines 5-9. The variable q is 1, 2, 3, or 4. . See Appellants specification page 15, lines 11-12.

The invention also includes pharmaceutically acceptable salts of formula I or oxidized derivatives of formula I and methyl, ethyl, propyl, isopropyl, butyl, isobutyl, pentyl ester or phenyl C_1-C_5 alkyl esters of formula I. See Appellants specification page 19, line 4 through page 20, line 20 and page 21, lines 12-16.

Claims 2-10 define preferred combinations of moieties "A" and "B". Claim 11 defines preferred "L" bridging groups and claim 12 defines the exemplified compounds. Claims 24 and 30 define preferred compounds of formula I where "B" is phenyl and claims 25-29 further define preferred compounds in specifying values for other moieties.

The invention also includes pharmaceutical compositions as defined in claim 13 which comprise an effective amount of a compound of formula I and a physiologically acceptable carrier. See Appellants specification page 30, lines 1-20.

(vi) GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

The following ground for rejection is presented for review on appeal:

Rejection of Claims 1-13 and 24-30 under 35 U.S.C. § 112, first paragraph, as allegedly not enabled.

(vii) ARGUMENT

Rejection of Claims 1-13 and 24-30 under 35 U.S.C. § 112, first paragraph, as allegedly not enabled.

Claims 24-30

- It is acknowledged in the office action that the specification provides enablement for using compounds of formula I where B is phenyl. Claims 24-30 define compounds and methods where B= phenyl such that the rejection of these claims should be withdrawn. Once this rejection is withdrawn, there will be no viable outstanding rejection of these claims. Therefore, Applicants respectfully submit claims 24-30 are presently allowable. Applicants also submit claim 12 is allowable in that it is directed to the compounds exemplified. For substantially all of the compounds listed, B is phenyl; however, there is one compound where B is quinolinyl. It is 4-[(5-{[(2,3-dihydro-1H-inden-5-ylamino)carbonyl]amino}quinolin-8-yl)oxy]-N-methylpyridine-2-

carboxamide. See example 87 of Appellant specification. This example is evidence the specification is enabling for compounds where B is other than phenyl.

Claims 1-13

These claims are directed to compounds of formula I below and compositions thereof where B is phenyl, pyridinyl or naphthyl.

Applicants maintain no evidence has been presented to refute the teachings within the specification such that it is objectively enabling for the full scope of compounds of formula I.

The specification provides ample guidance as to how to prepare the full scope of compounds of formula I (See pages 21-29 and pages 51-127), how to prepare pharmaceutical compositions with such compounds (pages 30-40), how to administer pharmaceutical compositions with such compounds of formula I (pages 43-44) and how to test such compounds for physiological activity related to the treatment of cancers(pages 128-129).

Since the structure of the claimed ureas is clearly defined by formula I, applicants maintain one of ordinary skill in art could synthesize these ureas without undue experimentation relying only on conventional methods known in the art, such as those disclosed on page 27 of the application. The synthesis of ureas is well known such that one skilled in the art would recognize the appropriate starting materials (substituted anilines and substituted nitro-aryls) necessary to prepare the claimed compounds without any guidance from the specification. However, general preparative methods for synthesizing ureas **are** given on pages 21-26. Guidance on the selection of starting materials and reaction conditions is provided by the specific preparations of the citations provided on page 27 and further guidance is provided by the disclosure and examples that appear on pages 51-127.

Based on the disclosure within the specification and conventional methods known in the art, one of ordinary skill in the art clearly would be able to prepare the claimed compounds without undue experimentation. No evidence has been presented to the contrary.

As to using the compounds of claims 1-13, 15-17, 22, 24-30, the specification is clearly objectively enabling in disclosing that the compounds have pharmacological activity on page 1,

lines 10-14; page 10, lines 3-13, pages 30-45; and are active in inhibiting raf based on the raf kinase assays disclosed on pages 127-129. It is recognized in the art that inhibition of raf kinase is correlated with the inhibition of growth of a variety of human tumor types, as discussed in citations mentioned in the specification on page 1, line 20 to page 2, line 3. Therefore, the inhibition of raf kinase correlates with the treatment of various tumors.

Examples of specific cancers (tumors) which can be treated are disclosed on pages 41-43. Dosage ranges and how to administer these compositions in the treatment of various conditions are described on pages 43-44. The specification also provides assays for determining the activity levels of the compounds on pages 128-129. One of ordinary skill in the art by performing the same assays described in the specification or similar tests, can, by routine experimentation, determine the activity levels of each of the claimed compounds in treating the various conditions known in the art to be correlated with raf inhibition. This is absolutely routine in the field.

The distinctions in chemical properties between the phenyl rings and pyridinyl or naphthyl rings do not diminish the enabling teachings within the specification. The examiner provides no basis why one skilled in the art could not make the full scope of compounds of formula I, test the pharmacological activity (raf inhibition) of these compounds, prepare pharmaceutical compositions with these compounds, and administer these compounds.

Ureas having naphthyl or pyridinyl groups bound directly to the urea group were known in the art and disclosed in WO 99/32436 and WO 99/32106, cited on page 27 of the specification. WO 99/32116 discloses about 30 compounds where pyridinyl is bound directly to the urea group (See examples 14, 16, 24, 46, 49, 50, 161-163, 166, 172, 198, 199, 201, 202-205, 208, 220, 222-227, 233, 236, 259, 276, 293, 353-357) and WO 99/32436 provides 12 compounds where naphthyl is bound to directly to the urea group (see examples 28 and 120-130). Similarly, the following publications and patents describe methods for preparing ureas where "B" is naphthyl: WO 00/55152, WO 00/55139, WO 02/083628, U.S. 6,297,381 and U.S. 6,525,046. The synthesis procedures described in the specification are similar to those described in WO 99/32436 and WO 99/32106, which are incorporated by reference in the subject application. In addition, the synthesis methods described in

these applications are similar to the syntheses disclosed in the specification and further illustrate the disclosure within the application is enabling. Synthesis of a compound where B is naphthyl or pyridinyl would simply require the appropriate selection of starting materials for the synthesis procedures described in the specification. The prior art syntheses of ureas where B is naphthyl or pyridinyl using similar methods to those disclosed in the specification is evidence that the specification provides sufficient disclosure for one skilled in the art to synthesize compounds of formula I where B is naphthyl or pyridinyl without undue experimentation.

Some experimentation may be required to achieve this objectives of this invention, but there is no evidence such experimentation would be undue in view of the detailed disclosure provided in the specification. Given the extent of the disclosure provided, it would at most involve routine experimentation if any at all, for one of ordinary skill in the art to make and use compounds of formula I where B is pyridinyl or naphthyl. This is clearly sufficient to satisfy the statute. See *Amgen v Hoechst Marion Roussel*, 314 F.2d 1313, 65 USPQ2d 1385 (Fed. Cir. 2003).

The examiner alleges it would require a large quantity of experimentation because these compounds would need to be synthesized and subjected to Applicant's raf biochemical assay. Given the extent of disclosure within the specification and the state of the art, these tasks would be routine.

Applicants draw attention to WO 99/32106 and WO 99/32436 to illustrate that preparing urea compounds with a pyridinyl or naphthyl moiety (B = naphthyl or pyridinyl) is possible and consistent with the teachings within the specification. Applicants agree that the examples disclosed in WO 99/32106 and WO 99/32436 are structurally distinct and provide no hint as to the activity of the compounds of formula I claimed herein. However, the disclosures within WO 99/32106 and WO 99/32436 illustrate it would be routine to test the compounds of formula I herein for raf kinase inhibition and rebut the Examiner's assumption that the pyridinyl moiety will negatively impact raf kinase inhibition. These disclosures provide a reasonable basis to conclude that compounds where "B" is pyridinyl or naphthyl will share the same biological properties as compounds where "B" is phenyl. Furthermore, through example 87, Applicants have shown that compounds where B is other than phenyl are raf kinase inhibitors.

Even absent the specification disclosures discussed above, the rejection of Claims 1-13 and 24-30 is clearly deficient in general under controlling case law. The courts have placed the burden upon the PTO to provide evidence shedding doubt on the disclosure that the invention can be made and used as stated; see, e.g., *In re Marzocchi*, 439 F.2d 220, 169 U.S.P.Q. 367 (CCPA 1971) (holding that how an enablement teaching is set forth, either by use of illustrative examples or by broad terminology, is of no importance.) The disclosure must be taken as in compliance with the enablement requirement of the first paragraph of § 112 unless there is reason to doubt the objective truth of the statements contained therein. See *In re Marzocchi*, supra. No such evidence or reason for doubting Applicants' disclosure has been provided. Only general statements and conclusions are made regarding the guidance provided with respect to the treatment of osteoporosis and inflammation.

For the reasons stated above, Applicants maintain that they have provided more than adequate guidance to enable the claimed invention and submit all pending claims meet the requirements of 35 U.S.C. §112, first paragraph.

It is respectfully submitted that there is ample basis to overturn the rejection of record in the Final Rejection, and the same is respectfully requested.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,

/Richard J. Traverso/
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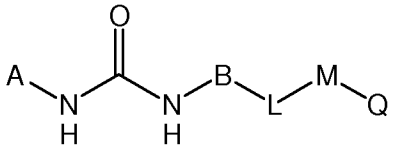
Attorney Docket No.: BAYER-0053
Date: February 13, 2010

xi) APPENDIX OF CLAIMS ON APPEAL

1) A compound of formula (I):

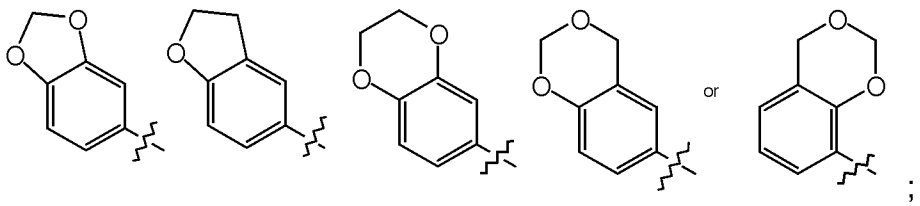


I

wherein

A is a bicyclic heterocycle which is:

(1) benzimidazolyl
(2) 1,3-benzothiazolyl
(3) 1,2,3-benzotriazolyl
(4) 1,3-benzoxazolyl
(5) 2,3-dihydro-1H-indolyl
(6) 2,3-dihydro-1H-indenyl
(7) 1,1-dioxido-2,3-dihydro-1-benzothienyl
(8) 1H-indazolyl
(9) 2H-indazolyl
(10) 1H-indolyl
(11) 2H-chromenyl
(12) quinoxalinyl or
(13) a group of the formula



;

optionally substituted with 1-4 substituents which are independently R^1, OR^1, $S(O)_pR^1$, $C(O)R^1$, $C(O)OR^1$, $C(O)NR^1R^2$, halogen, oxo, cyano, or nitro;

B is phenyl, naphthyl or pyridyl, optionally substituted with 1-4 substituents which are independently C_1-C_5 linear or branched alkyl, C_1-C_5 linear or branched haloalkyl, C_1-C_3 alkoxy, hydroxy, amino, C_1-C_3 alkylamino, C_1-C_6 dialkylamino, carboxyamide, halogen, cyano, nitro or $S(O)_pR^7$;

L is :

(a) $-(CH_2)_m-O-(CH_2)_l-$,
(b) $-(CH_2)_m-(CH_2)_l-$,
(c) $-(CH_2)_m-C(O)-(CH_2)_l-$,
(d) $-(CH_2)_m-NR^3-(CH_2)_l-$,
(e) $-(CH_2)_m- NR^3C(O)-(CH_2)_l-$,
(f) $-(CH_2)_m-S-(CH_2)_l-$,
(g) $-(CH_2)_m-C(O)NR^3-(CH_2)_l-$, or
(h) a single bond;

m and l are integers independently selected from 0-4;

M is a pyridine ring, optionally substituted with 1-3 substituents which are independently C_1-C_5 linear or branched alkyl, C_1-C_5 linear or branched haloalkyl, C_1-C_3 alkoxy, hydroxy, amino, C_1-C_3 alkylamino, C_1-C_6 dialkylamino, halogen, or nitro;.

Q is $C(O)R^4$, $C(O)OR^4$ or $C(O)NR^4R^5$;

each of R^1, R^2, R^3, R^4 and R^5 is independently:

(a) hydrogen,
(b) C_1-C_5 linear, branched, or cyclic alkyl,
(c) phenyl,
(d) C_1-C_3 alkyl-phenyl,
(e) up to per–halo substituted C_1-C_5 linear or branched alkyl,
(f) $-(CH_2)_q$-X, wherein X is a 5 or 6 membered heterocyclic ring, containing at least one atom selected from oxygen, nitrogen and sulfur, which is saturated, partially saturated, or aromatic, or a 8-10 membered bicyclic heteroaryl having 1-4 heteroatoms which are O, N or S, or
(g) $-(CH_2)_q$-Y, where Y is $C(O)R^6$, $C(O)OR^6$ and $C(O)NR^6R^7$;

each of R^6 – R^7 is independently :

(a) hydrogen,
(b) C_1-C_5 linear, branched, or cyclic alkyl,
(c) phenyl,
(d) C_1-C_3 alkyl-phenyl, or
(e) up to per–halo substituted C_1-C_5 linear or branched alkyl;

each of R^1, R^2, R^3, R^4 , R^5, R^6 and R^7, other than per–halo substituted C_1-C_5 linear or branched alkyl, is optionally substituted with 1-3 substituents which are independently C_1-C_5 linear or branched alkyl, up to perhalo substituted C_1-C_5 linear or branched alkyl, C_1-C_3 alkoxy, hydroxy, carboxy, amino, C_1-C_3 alkylamino, C_1-C_6 dialkylamino, halogen, cyano, or nitro;

p is an integer selected from 0, 1, or 2; and

q is an integer selected from 1, 2, 3, or 4

or a pharmaceutically acceptable salt of formula I or an oxidized derivative of formula I wherein one or more urea nitrogens are substituted with a hydroxyl group, or an oxidized derivative of formula I wherein the nitrogen atom of pyridine ring M is in the oxide form, or a methyl, ethyl, propyl, isopropyl, butyl, isobutyl, pentyl ester or phenyl C_1-C_5 alkyl ester of formula I at a carboxylic acid group or amide group.

2) A compound of claim 1 wherein A and B follow one of the following combinations:

A= 1H-benzimidazol-5-yl; and B= phenyl, pyridinyl or naphthyl,
A= 1H-benzimidazol-6-yl; and B= phenyl, pyridinyl or naphthyl,
A= 1,3-benzodioxin-6-yl; and B= phenyl, pyridinyl or naphthyl,
A= 1,3-benzodioxin-7-yl; and B= phenyl, pyridinyl or naphthyl,
A= 1,3-benzodioxin-8-yl; and B= phenyl, pyridinyl or naphthyl,
A= 1,3-benzodioxol-4-yl; and B= phenyl, pyridinyl or naphthyl,
A= 1,3-benzodioxol-5-yl; and B= phenyl, pyridinyl or naphthyl,
A= 1,3-benzothiazol-2-yl; and B= phenyl, pyridinyl or naphthyl,
A= 1,3-benzothiazol-5-yl; and B= phenyl, pyridinyl or naphthyl,
A= 1,3-benzothiazol-6-yl; and B= phenyl, pyridinyl or naphthyl,
A= 1,2,3-benzotriazol-5-yl; and B= phenyl, pyridinyl or naphthyl,
A= 1,3-benzoxazol-2-yl; and B= phenyl, pyridinyl or naphthyl, or
A= 1,3-benzoxazol-6-yl; and B= phenyl, pyridinyl or naphthyl.

3) A compound of claim 1 wherein A and B follow one of the following combinations:

A= 1H-benzimidazolyl; and B= phenyl or pyridinyl,

A= 1,3-benzodioxinyl; and B= phenyl or pyridinyl,

A= 1,3-benzodioxolyl; and B= phenyl or pyridinyl,

A= 1,3-benzothiazolyl; and B= phenyl or pyridinyl,

A= 1,2,3-benzotriazolyl; and B= phenyl or pyridinyl, or

A= 1,3-benzoxazolyl; and B= phenyl, pyridinyl.

4) A compound of claim 1 wherein A and B follow one of the following combinations:

A= 1H-benzimidazol-5-yl; and B= phenyl or pyridinyl,

A= 1H-benzimidazol-6-yl; and B= phenyl or pyridinyl,

A= 1,3-benzodioxin-6-yl; and B= phenyl or pyridinyl,,

A= 1,3-benzodioxin-7-yl; and B= phenyl or pyridinyl,

A= 1,3-benzodioxin-8-yl; and B= phenyl or pyridinyl,

A= 1,3-benzodioxol-4-yl; and B= phenyl or pyridinyl, ,

A= 1,3-benzodioxol-5-yl; and B= phenyl or pyridinyl,

A= 1,3-benzothiazol-2-yl; and B= phenyl or pyridinyl,

A= 1,3-benzothiazol-5-yl; and B= phenyl or pyridinyl,

A= 1,3-benzothiazol-6-yl; and B= phenyl or pyridinyl,

A= 1,2,3-benzotriazol-5-yl; and B= phenyl or pyridinyl,

A= 1,3-benzoxazol-2-yl; and B= phenyl or pyridinyl, or

A= 1,3-benzoxazol-6-yl; and B= phenyl or pyridinyl.

5) A compound of claim 1 wherein A and B follow one of the following combinations:

A= 2,3-dihydro-1,4-benzodioxin-5-yl; and B= phenyl, pyridinyl or naphthyl,

A= 2,3-dihydro-1,4-benzodioxin-6-yl; and B= phenyl, pyridinyl or naphthyl,

A= 2,3-dihydro-1-benzofuran-5-yl; and B= phenyl, pyridinyl or naphthyl,

A= 2,3-dihydro-1H-indol-5-yl; and B= phenyl, pyridinyl or naphthyl,

A= 2,3-dihydro-1H-indol-6-yl; and B= phenyl, pyridinyl or naphthyl,

A= 2,3-dihydro-1H-inden-4-yl; and B= phenyl, pyridinyl or naphthyl,

A= 2,3-dihydro-1H-inden-5-yl; and B= phenyl, pyridinyl or naphthyl,

A= 1,1-dioxido-2,3-dihydro-1-benzothien-6-yl; and B= phenyl, pyridinyl or naphthyl.

6) A compound of claim 1 wherein A and B follow one of the following combinations:

A= 2,3-dihydro-1,4-benzodioxin-5-yl; and B= phenyl or pyridinyl,

A= 2,3-dihydro-1,4-benzodioxin-6-yl; and B= phenyl or pyridinyl,

A= 2,3-dihydro-1-benzofuran-5-yl; and B= phenyl or pyridinyl,

A= 2,3-dihydro-1H-indol-5-yl; and B= phenyl or pyridinyl,

A= 2,3-dihydro-1H-indol-6-yl; and B= phenyl or pyridinyl,

A= 2,3-dihydro-1H-inden-4-yl; and B= phenyl or pyridinyl,

A= 2,3-dihydro-1H-inden-5-yl; and B= phenyl or pyridinyl, or

A= 1,1-dioxido-2,3-dihydro-1-benzothien-6-yl; and B= phenyl or pyridinyl.

7) A compound of claim 1 wherein A and B follow one of the following combinations:

A= 1H-indazol-5-yl; and B= phenyl, pyridinyl or naphthyl,

A= 2H-indazol-5-yl; and B= phenyl, pyridinyl or naphthyl,

A= 1H-indazol-6-yl; and B= phenyl, pyridinyl or naphthyl,

A= 1H-indol-5-yl; and B= phenyl, pyridinyl or naphthyl,

A= 2-oxo-2H-chromen-7-yl; and B= phenyl, pyridinyl or naphthyl or

A= 1-oxo-2,3-dihydro-1H-inden-5-yl; and B= phenyl, pyridinyl or naphthyl.

8) A compound of claim 1 wherein A and B follow one of the following combinations:

A= 1H-indazol-5-yl; and B= phenyl or pyridinyl,
A= 2H-indazol-5-yl; and B= phenyl or pyridinyl,
A= 1H-indazol-6-yl; and B= phenyl or pyridinyl,
A= 1H-indol-5-yl; and B= phenyl or pyridinyl,
A= 2-oxo-2H-chromen-7-yl; and B= phenyl or pyridinyl, or
A= 1-oxo-2,3-dihydro-1H-inden-5-yl; and B= phenyl or pyridinyl.

9) A compound of claim 1 wherein A and B follow one of the following combinations:

A= quinoxalin-2-yl; and B= phenyl, pyridinyl or naphthyl or
A= quinoxalin-6-yl; and B= phenyl , pyridinyl or naphthyl.

10) A compound of claim 1 wherein A and B follow one of the following combinations:

A= quinoxalin-2-yl; and B= phenyl or pyridinyl, or
A= quinoxalin-6-yl; and B= phenyl or pyridinyl.

11) A compound as in claim 1 wherein L is -O- or –S-.

12) (previously presented) A compound which is:

- N-methyl-4-[3-({[(2-methyl-1,3-benzoxazol-6-yl)amino]carbonyl}amino)phenoxy]pyridine-2-carboxamide

- 4-[4-({[(1-acetyl-2,3-dihydro-1H-indol-6-yl)amino]carbonyl}amino)phenoxy]-N-methylpyridine-2-carboxamide
- 4-[4-({[(6-chloro-1,3-benzothiazol-2-yl)amino]carbonyl}amino)phenoxy]-N-methylpyridine-2-carboxamide
- N-methyl-4-{4-[({[6-(trifluoromethoxy)-1,3-benzothiazol-2-yl]amino}carbonyl)amino]phenoxy}pyridine-2-carboxamide
- 4-[4-({[(6-fluoro-1,3-benzothiazol-2-yl)amino]carbonyl}amino)phenoxy]-N-methylpyridine-2-carboxamide
- 4-[3-fluoro-4-({[(6-fluoro-1,3-benzothiazol-2-yl)amino]carbonyl}amino)phenoxy]-N-methylpyridine-2-carboxamide
- 4-{3-fluoro-4-[({[6-(trifluoromethoxy)-1,3-benzothiazol-2-yl]amino}carbonyl)amino]phenoxy}-N-methylpyridine-2-carboxamide;
- 4-[4-({[(6-methoxy-1,3-benzothiazol-2-yl)amino]carbonyl}amino)phenoxy]-N-methylpyridine-2-carboxamide
- 4-[4-({[(6-methoxy-1,3-benzothiazol-2-yl)amino]carbonyl}amino)phenoxy]-N-methylpyridine-2-carboxamide
- 4-[4-({[(5-chloro-1,3-benzoxazol-2-yl)amino]carbonyl}amino)phenoxy]-N-methylpyridine-2-carboxamide
- 4-[4-({[(5-chloro-1,3-benzoxazol-2-yl)amino]carbonyl}amino)phenoxy]-N-methylpyridine-2-carboxamide
- 4-[4-({[(6-chloro-1,3-benzothiazol-2-yl)amino]carbonyl}amino)-3-fluorophenoxy]-N-methylpyridine-2-carboxamide
- 4-[4-({[(6-chloro-1,3-benzothiazol-2-yl)amino]carbonyl}amino)-3-fluorophenoxy]-N-methylpyridine-2-carboxamide
- 4-(2-chloro-4-{[(2,3-dihydro-1H-inden-5-ylamino)carbonyl]amino}phenoxy)-N-methylpyridine-2-carboxamide
- 4-[(5-{[(2,3-dihydro-1H-inden-5-ylamino)carbonyl]amino}quinolin-8-yl)oxy]-N-methylpyridine-2-carboxamide

- 4-[4-({[(4,6-difluoro-1,3-benzothiazol-2-yl)amino]carbonyl}amino)-3-fluorophenoxy]-N-methylpyridine-2-carboxamide
- 4-[3-fluoro-4-({[(6-methoxy-1,3-benzothiazol-2-yl)amino]carbonyl}amino)phenoxy]-N-methylpyridine-2-carboxamide
- 4-(4-{[({1-[2-(diethylamino)ethyl]-1H-indol-5-yl}amino)carbonyl]amino}-3-fluorophenoxy)-N-methylpyridine-2-carboxamide;
- 4-(4-{[(2,3-dihydro-1H-inden-5-ylamino)carbonyl]amino}-3-fluorophenoxy)-N-methylpyridine-2-carboxamide
- 4-[3-fluoro-4-({[(1-oxo-2,3-dihydro-1H-inden-5-yl)amino]carbonyl}amino)phenoxy]-N-methylpyridine-2-carboxamide
- 4-[4-({[(1,1-dioxido-2,3-dihydro-1-benzothien-6-yl)amino]carbonyl}amino)-3-fluorophenoxy]-N-methylpyridine-2-carboxamide
- 4-[3-fluoro-4-({[(1-methyl-1H-indazol-5-yl)amino]carbonyl}amino)phenoxy]-N-methylpyridine-2-carboxamide
- 4-[2-fluoro-4-({[(1-methyl-1H-indazol-5-yl)amino]carbonyl}amino)phenoxy]-N-methylpyridine-2-carboxamide
- 4-[2,4-difluoro-5-({[(1-methyl-1H-indazol-5-yl)amino]carbonyl}amino)phenoxy]-N-methylpyridine-2-carboxamide
- N-methyl-4-[4-({[(1-methyl-1H-indazol-5-yl)amino]carbonyl}amino)-3-(trifluoromethyl)-phenoxy]pyridine-2-carboxamide
- 4-[4-fluoro-3-({[(1-methyl-1H-indazol-5-yl)amino]carbonyl}amino)phenoxy]-N-methylpyridine-2-carboxamide
- 4-[2-fluoro-5-({[(1-methyl-1H-indazol-5-yl)amino]carbonyl}amino)phenoxy]-N-methylpyridine-2-carboxamide
- 4-[2-chloro-6-fluoro-4-({[(1-methyl-1H-indazol-5-yl)amino]carbonyl}amino)phenoxy]-N-methylpyridine-2-carboxamide
- 4-[3-fluoro-4-({[(1-methyl-1H-indazol-5-yl)amino]carbonyl}amino)phenoxy]-N-(2-methoxyethyl)pyridine-2-carboxamide

- 4-[3-fluoro-4-({[(2,2,3,3-tetrafluoro-2,3-dihydro-1,4-benzodioxin-6-yl)amino]carbonyl}-amino)phenoxy]-N-methylpyridine-2-carboxamide
- 4-[4-({[(2,2-difluoro-1,3-benzodioxol-5-yl)amino]carbonyl}amino)-3-fluorophenoxy]-N-methylpyridine-2-carboxamide
- N-methyl-4-(4-{[(quinoxalin-6-ylamino)carbonyl]amino}phenoxy)pyridine-2-carboxamide
- 4-(3-fluoro-4-{[(quinoxalin-6-ylamino)carbonyl]amino}phenoxy)-N-methylpyridine-2-carboxamide
- N-methyl-4-[4-{[(quinoxalin-6-ylamino)carbonyl]amino}-3-(trifluoromethyl)phenoxy]-pyridine-2-carboxamide
- 4-(3-chloro-4-{[(quinoxalin-6-ylamino)carbonyl]amino}phenoxy)-N-methylpyridine-2-carboxamide
- N-methyl-4-[4-({[(2,2,3,3-tetrafluoro-2,3-dihydro-1,4-benzodioxin-6-yl)amino]carbonyl}-amino)-3-(trifluoromethyl)phenoxy]pyridine-2-carboxamide
- 4-[4-({[(2-methyl-1,3-benzothiazol-5-yl)amino]carbonyl}amino)phenoxy]pyridine-2-carboxamide
- N-methyl-4-[4-({[(2-methyl-1,3-benzothiazol-5-yl)amino]carbonyl}amino)-3-(trifluoro-methyl)phenoxy]pyridine-2-carboxamide
- N-methyl-4-[3-methyl-4-({[(4-methyl-2-oxo-2H-chromen-7-yl)amino]carbonyl}amino)-phenoxy]pyridine-2-carboxamide
- N-methyl-4-[3-methyl-4-({[(2-methyl-1,3-benzothiazol-5-yl)amino]carbonyl}amino)-phenoxy]pyridine-2-carboxamide
- 4-[3-fluoro-4-({[(2-methyl-1,3-benzothiazol-5-yl)amino]carbonyl}amino)phenoxy]-N-methylpyridine-2-carboxamide
- N-methyl-4-{[3-({[(1-methyl-1H-indazol-5-yl)amino]carbonyl}amino)phenoxy]methyl}-pyridine-2-carboxamide
- 4-{[3-fluoro-4-({[(1-methyl-1H-indazol-5-yl)amino]carbonyl}amino)phenoxy]methyl}-N-methylpyridine-2-carboxamide
- 4-[2-chloro-4-({[(1-methyl-1H-indazol-5-yl)amino]carbonyl}amino)phenoxy]-N-methylpyridine-2-carboxamide

- N-methyl-4-[3-({[(2,2,3,3-tetrafluoro-2,3-dihydro-1,4-benzodioxin-6-yl)amino]carbonyl}-amino)phenoxy]pyridine-2-carboxamide
- N-methyl-4-[4-({[(2,2,3,3-tetrafluoro-2,3-dihydro-1,4-benzodioxin-6-yl)amino]carbonyl}-amino)phenoxy]pyridine-2-carboxamide
- 4-[3-({[(2,2-difluoro-1,3-benzodioxol-5-yl)amino]carbonyl}amino)phenoxy]-N-methylpyridine-2-carboxamide
- 4-[4-({[(2,2-difluoro-1,3-benzodioxol-5-yl)amino]carbonyl}amino)phenoxy]-N-methylpyridine-2-carboxamide
- 4-[2-chloro-4-({[(2,2,3,3-tetrafluoro-2,3-dihydro-1,4-benzodioxin-6-yl)amino]carbonyl}-amino)phenoxy]-N-methylpyridine-2-carboxamide
- 4-[2-chloro-4-({[(2,2-difluoro-1,3-benzodioxol-5-yl)amino]carbonyl}amino)phenoxy]-N-methylpyridine-2-carboxamide
- 4-[3-chloro-4-({[(1-methyl-1H-indazol-5-yl)amino]carbonyl}amino)phenoxy]-N-methylpyridine-2-carboxamide
- N-methyl-4-[3-({[(1-methyl-1H-indazol-5-yl)amino]carbonyl}amino)phenoxy]pyridine-2-carboxamide
- N-methyl-4-[3-({[(1-methyl-1H-indazol-6-yl)amino]carbonyl}amino)phenoxy]pyridine-2-carboxamide
- 4-(3-{[(2,3-dihydro-1-benzofuran-5-ylamino)carbonyl]amino}phenoxy)-N-methylpyridine-2-carboxamide
- N-methyl-4-{3-[({[2-(trifluoromethyl)-1H-benzimidazol-5-yl]amino}carbonyl)amino]-phenoxy}pyridine-2-carboxamide
- 4-[4-chloro-3-({[(1-methyl-1H-indazol-5-yl)amino]carbonyl}amino)phenoxy]-N-methyl-pyridine-2-carboxamide
- 4-[4-chloro-3-({[(2,2,3,3-tetrafluoro-2,3-dihydro-1,4-benzodioxin-6-yl)amino]-carbonyl}amino)phenoxy]-N-methylpyridine-2-carboxamide
- 4-[4-chloro-3-({[(2,2-difluoro-1,3-benzodioxol-5-yl)amino]carbonyl}amino)phenoxy]-N-methylpyridine-2-carboxamide

- 4-[3-chloro-4-({[(1-methyl-1H-indazol-5-yl)amino]carbonyl}amino)phenoxy]pyridine-2-carboxamide
- 4-[2-chloro-4-({[(1-methyl-1H-indazol-5-yl)amino]carbonyl}amino)phenoxy]pyridine-2-carboxamide
- 4-[4-({[(2,2-difluoro-1,3-benzodioxol-5-yl)amino]carbonyl}amino)-3-fluorophenoxy]-pyridine-2-carboxamide
- 4-[3-fluoro-4-({[(2,2,3,3-tetrafluoro-2,3-dihydro-1,4-benzodioxin-6-yl)amino]carbonyl}-amino)phenoxy]pyridine-2-carboxamide
- 4-(4-{[(2,3-dihydro-1H-inden-5-ylamino)carbonyl]amino}phenoxy)-N-methylpyridine-2-carboxamide
- N-methyl-4-[4-({[(1-oxo-2,3-dihydro-1H-inden-5-yl)amino]carbonyl}amino)phenoxy]-pyridine-2-carboxamide
- 5-[3-fluoro-4-({[(2,2,3,3-tetrafluoro-2,3-dihydro-1,4-benzodioxin-6-yl)amino]carbonyl}-amino)phenoxy]-N-methylnicotinamide
- 4-[4-{[(2,3-dihydro-1H-inden-5-ylamino)carbonyl]amino}-3-(trifluoromethyl)phenoxy]-N-methylpyridine-2-carboxamide
- N-methyl-4-[4-({[(1-oxo-2,3-dihydro-1H-inden-5-yl)amino]carbonyl}amino)-3-(trifluoromethyl)phenoxy]pyridine-2-carboxamide
- 4-(3-chloro-4-{[(2,3-dihydro-1H-inden-5-ylamino)carbonyl]amino}phenoxy)pyridine-2-carboxamide
- 4-[3-chloro-4-({[(1-oxo-2,3-dihydro-1H-inden-5-yl)amino]carbonyl}amino)phenoxy]-pyridine-2-carboxamide
- N-methyl-4-[4-({[(1-methyl-1H-indazol-6-yl)amino]carbonyl}amino)phenoxy]pyridine-2-carboxamide
- 4-(4-{[(1,3-benzothiazol-6-ylamino)carbonyl]amino}phenoxy)-N-methylpyridine-2-carboxamide
- N-methyl-4-[4-({[(1-methyl-1H-indazol-5-yl)amino]carbonyl}amino)phenoxy]pyridine-2-carboxamide

- 4-(4-{[(2,3-dihydro-1-benzofuran-5-ylamino)carbonyl]amino}phenoxy)-N-methylpyridine-2-carboxamide
- 4-[2,4-dichloro-5-({[(2,2,3,3-tetrafluoro-2,3-dihydro-1,4-benzodioxin-6-yl)amino]carbonyl}-amino)phenoxy]-N-methylpyridine-2-carboxamide
- 4-[2,4-dichloro-5-({[(1-methyl-1H-indazol-5-yl)amino]carbonyl}amino)phenoxy]-N-methylpyridine-2-carboxamide
- 4-[3-chloro-4-({[(2,2-difluoro-1,3-benzodioxol-5-yl)amino]carbonyl}amino)phenoxy]-N-methylpyridine-2-carboxamide
- 4-[3-chloro-4-({[(2,2,3,3-tetrafluoro-2,3-dihydro-1,4-benzodioxin-6-yl)amino]carbonyl}-amino)phenoxy]-N-methylpyridine-2-carboxamide;
- 4-(3-chloro-4-{[(2,3-dihydro-1H-inden-5-ylamino)carbonyl]amino}phenoxy)-N-methylpyridine-2-carboxamide
- 4-(3-chloro-4-{[(2,3-dihydro-1H-inden-5-ylamino)carbonyl]amino}phenoxy)-N-methylpyridine-2-carboxamide;
- 4-[3-chloro-4-({[(1-oxo-2,3-dihydro-1H-inden-5-yl)amino]carbonyl}amino)phenoxy]-N-methylpyridine-2-carboxamide;
- 4-[2-chloro-4-({[(1-oxo-2,3-dihydro-1H-inden-5-yl)amino]carbonyl}amino)phenoxy]-N-methylpyridine-2-carboxamide
- 4-(3-chloro-4-{[(2,3-dihydro-1H-inden-5-ylamino)carbonyl]amino}phenoxy)-N-methylpyridine-2-carboxamide
- 4-(3-chloro-4-{[(2,3-dihydro-1H-inden-5-ylamino)carbonyl]amino}phenoxy)-N-methylpyridine-2-carboxamide
- 4-[2,4-dichloro-5-({[(2,2-difluoro-1,3-benzodioxol-5-yl)amino]carbonyl}amino)phenoxy]-N-methylpyridine-2-carboxamide
- N-methyl-4-{4-[({[1-(methylsulfonyl)-2,3-dihydro-1H-indol-5-yl]amino}carbonyl)amino]-phenoxy}pyridine-2-carboxamide
- N-methyl-4-[3-nitro-4-({[(2,2,3,3-tetrafluoro-2,3-dihydro-1,4-benzodioxin-6-yl)amino]-carbonyl}amino)phenoxy]pyridine-2-carboxamide

- N-methyl-4-[2-methyl-4-({[(2,2,3,3-tetrafluoro-2,3-dihydro-1,4-benzodioxin-6-yl)amino]-carbonyl}amino)phenoxy]pyridine-2-carboxamide
- 4-[2,3-difluoro-4-({[(2,2,4,4-tetrafluoro-4H-1,3-benzodioxin-6-yl)amino]carbonyl}amino)-phenoxy]-N-methylpyridine-2-carboxamide
- 4-[3,5-difluoro-4-({[(2,2,4,4-tetrafluoro-4H-1,3-benzodioxin-6-yl)amino]carbonyl}amino)-phenoxy]-N-methylpyridine-2-carboxamide
- 4-[2,5-difluoro-4-({[(2,2,4,4-tetrafluoro-4H-1,3-benzodioxin-6-yl)amino]carbonyl}amino)-phenoxy]-N-methylpyridine-2-carboxamide
- N-methyl-4-[4-({[(2,2,3,3-tetrafluoro-2,3-dihydro-1,4-benzodioxin-5-yl)amino]carbonyl}-amino)phenoxy]pyridine-2-carboxamide trifluoroacetate
- 4-[3-fluoro-4-({[(2,2,4,4-tetrafluoro-4H-1,3-benzodioxin-6-yl)amino]carbonyl}-amino)phenoxy]-pyridine-2-carboxamide
- 4-[3-fluoro-4-({[(2,2,4,4-tetrafluoro-4H-1,3-benzodioxin-6-yl)amino]carbonyl}amino)-phenoxy]pyridine-2-carboxamide
- N-methyl-4-{[5-({[(2,2,4,4-tetrafluoro-4H-1,3-benzodioxin-6-yl)amino]carbonyl}amino)-quinolin-8-yl]oxy}pyridine-2-carboxamide
- 4-(3-{[(1H-indazol-5-ylamino)carbonyl]amino}phenoxy)-N-methylpyridine-2-carboxamide dihydrochloride
- N-[2-(methylamino)-2-oxoethyl]-4-[4-({[(2,2,4,4-tetrafluoro-4H-1,3-benzodioxin-6-yl)amino]carbonyl}amino)phenoxy]pyridine-2-carboxamide
- 4-(3-fluoro-4-{[(quinoxalin-2-ylamino)carbonyl]amino}phenoxy)-N-methylpyridine-2-carboxamide
- N-[2-(dimethylamino)-2-oxoethyl]-4-[4-({[(2,2,4,4-tetrafluoro-4H-1,3-benzodioxin-6-yl)amino]carbonyl}amino)phenoxy]pyridine-2-carboxamide
- N-methyl-4-[3-methyl-4-({[(2,2,4,4-tetrafluoro-4H-1,3-benzodioxin-6-yl)amino]carbonyl}-amino)phenoxy]pyridine-2-carboxamide
- Methyl 4-[3-({[(2,2,4,4-tetrafluoro-4H-1,3-benzodioxin-7-yl)amino]carbonyl}-amino)phenoxy]-pyridine-2-carboxylate

- 4-[3-chloro-4-({[(2,2,4,4-tetrafluoro-4H-1,3-benzodioxin-6yl)amino]carbonyl}amino)-phenoxy]-N-methylpyridine-2-carboxamide
- 4-[3-chloro-4-({[(2,2,4,4-tetrafluoro-4H-1,3-benzodioxin-6-yl)amino]carbonyl}amino)-phenoxy]pyridine-2-carboxamide
- 4-(3-{[(1,3-benzodioxol-5-ylamino)carbonyl]amino}phenoxy)-N-methylpyridine-2-carboxamide
- N-methyl-4-[3-({[(2,2,4,4-tetrafluoro-4H-1,3-benzodioxin-6-yl)amino]carbonyl}amino)-phenoxy]pyridine-2-carboxamide
- 4-(3-{[(2,3-dihydro-1,4-benzodioxin-6-ylamino)carbonyl]amino}phenoxy)-N-methylpyridine-2-carboxamide
- 4-[4-chloro-3-({[(2,2,4,4-tetrafluoro-4H-1,3-benzodioxin-6-yl)amino]carbonyl}amino)-phenoxy]-N-methylpyridine-2-carboxamide
- 5-[2-fluoro-4-({[(2,2,4,4-tetrafluoro-4H-1,3-benzodioxin-6-yl)amino]carbonyl}amino)-phenoxy]-N-methylnicotinamide
- 4-[2-chloro-4-({[(2,2,4,4-tetrafluoro-4H-1,3-benzodioxin-6-yl)amino]carbonyl}amino)-phenoxy]pyridine-2-carboxamide
- 4-[3-chloro-4-({[(2,2,4,4-tetrafluoro-4H-1,3-benzodioxin-6-yl)amino]carbonyl}amino)-phenoxy]pyridine-2-carboxamide
- 4-[3-fluoro-4-({[(2,2,4,4-tetrafluoro-4H-1,3-benzodioxin-6-yl)amino]carbonyl}amino)-phenoxy]pyridine-2-carboxamide
- 4-[3-fluoro-4-({[(2,2,4,4-tetrafluoro-4H-1,3-benzodioxin-6-yl)amino]carbonyl}amino)-phenoxy]pyridine-2-carboxamide
- 4-(3-{[(1,3-benzodioxol-5-ylamino)carbonyl]amino}-4-chlorophenoxy)-N-methylpyridine-2-carboxamide
- 4-[4-chloro-3-({[(6-fluoro-4H-1,3-benzodioxin-8-yl)amino]carbonyl}amino)phenoxy]-N-methylpyridine-2-carboxamide
- 4-(4-{[(1,3-benzodioxol-5-ylamino)carbonyl]amino}-3-fluorophenoxy)pyridine-2-carboxamide

- 4-[3-fluoro-4-({[(6-fluoro-4H-1,3-benzodioxin-8-yl)amino]carbonyl}amino)phenoxy]-pyridine-2-carboxamide
- 4-(4-chloro-3-{[(2,3-dihydro-1,4-benzodioxin-6-ylamino)carbonyl]amino}phenoxy)-N-methylpyridine-2-carboxamide
- 4-[3-({[(7-fluoro-2,3-dihydro-1,4-benzodioxin-5-yl)amino]carbonyl}amino)phenoxy]-N-methylpyridine-2-carboxamide
- 4-[3-fluoro-4-({[(2,2,4,4-tetrafluoro-4H-1,3-benzodioxin-6-yl)amino]carbonyl}amino)-phenoxy]-N-methylpyridine-2-carboxamide
- 4-(4-{[(1,3-benzodioxol-5-ylamino)carbonyl]amino}phenoxy)-N-methylpyridine-2-carboxamide
- N-methyl-4-[4-({[(2,2,4,4-tetrafluoro-4H-1,3-benzodioxin-6-yl)amino]carbonyl}amino)-phenoxy]pyridine-2-carboxamide
- Methyl 4-[4-({[(2,2,4,4-tetrafluoro-4H-1,3-benzodioxin-6-yl)amino]carbonyl}-amino)phenoxy]pyridine-2-carboxylate
- Methyl 5-[4-({[(2,2,4,4-tetrafluoro-4H-1,3-benzodioxin-6-yl)amino]carbonyl}amino)-phenoxy]nicotinate
- 4-[2,4-dichloro-5-({[(2,2,4,4-tetrafluoro-4H-1,3-benzodioxin-6-yl)amino]carbonyl}amino)-phenoxy]-N-methylpyridine-2-carboxamide
- N-methyl-5-[4-({[(2,2,4,4-tetrafluoro-4H-1,3-benzodioxin-6-yl)amino]carbonyl}amino)-phenoxy]nicotinamide
- 4-(4-{[(1,3-benzodioxol-5-ylamino)carbonyl]amino}-3-chlorophenoxy)-N-methylpyridine-2-carboxamide
- 4-[3-chloro-4-({[(6-fluoro-4H-1,3-benzodioxin-8-yl)amino]carbonyl}amino)phenoxy]-N-methylpyridine-2-carboxamide
- N-methyl-4-[2-methyl-4-({[(2,2,4,4-tetrafluoro-4H-1,3-benzodioxin-6-yl)amino]carbonyl}-amino)phenoxy]pyridine-2-carboxamide
- N-methyl-4-[3-nitro-4-({[(2,2,4,4-tetrafluoro-4H-1,3-benzodioxin-6-yl)amino]carbonyl}-amino)phenoxy]pyridine-2-carboxamide

- N-methyl-4-[3-({[(2,2,4,4-tetrafluoro-4H-1,3-benzodioxin-6-yl)amino]carbonyl}amino)-phenoxy]pyridine-2-carboxamide 1-oxide
- 4-[3-({[(1-methyl-1H-indazol-5-yl)amino]carbonyl}amino)phenoxy]-N-(2-piperidin-1-ylethyl)pyridine-2-carboxamide
- 4-[3-({[(1-methyl-1H-indazol-5-yl)amino]carbonyl}amino)phenoxy]-N-(2-pyrrolidin-1-ylethyl)pyridine-2-carboxamide
- 4-[3-({[(1-methyl-1H-indazol-5-yl)amino]carbonyl}amino)phenoxy]-N-pyridin-3-ylpyridine-2-carboxamide
- N-[3-(1H-imidazol-1-yl)propyl]-4-[3-({[(1-methyl-1H-indazol-5-yl)amino]carbonyl}amino)-phenoxy]pyridine-2-carboxamide
- N-(2-piperidin-1-ylethyl)-4-[3-({[(2,2,4,4-tetrafluoro-4H-1,3-benzodioxin-6-yl)amino]-carbonyl}amino)phenoxy]pyridine-2-carboxamide
- N-(2-pyrrolidin-1-ylethyl)-4-[3-({[(2,2,4,4-tetrafluoro-4H-1,3-benzodioxin-6-yl)amino]-carbonyl}amino)phenoxy]pyridine-2-carboxamide
- N-pyridin-3-yl-4-[3-({[(2,2,4,4-tetrafluoro-4H-1,3-benzodioxin-6-yl)amino]carbonyl}-amino)phenoxy]pyridine-2-carboxamide
- N-[3-(1H-imidazol-1-yl)propyl]-4-[3-({[(2,2,4,4-tetrafluoro-4H-1,3-benzodioxin-6-yl)amino]-carbonyl}amino)phenoxy]pyridine-2-carboxamide
- N-[3-(1H-imidazol-1-yl)propyl]-4-[4-({[(2,2,4,4-tetrafluoro-4H-1,3-benzodioxin-6-yl)amino]-carbonyl}amino)phenoxy]pyridine-2-carboxamide
- N-(2-pyrrolidin-1-ylethyl)-4-[4-({[(2,2,4,4-tetrafluoro-4H-1,3-benzodioxin-6-yl)amino]-carbonyl}amino)phenoxy]pyridine-2-carboxamide
- N-(2-piperidin-1-ylethyl)-4-[4-({[(2,2,4,4-tetrafluoro-4H-1,3-benzodioxin-6-yl)amino]-carbonyl}amino)phenoxy]pyridine-2-carboxamide
- N-(2-piperazin-1-ylethyl)-4-[4-({[(2,2,4,4-tetrafluoro-4H-1,3-benzodioxin-6-yl)amino]-carbonyl}amino)phenoxy]pyridine-2-carboxamide
- N-pyridin-2-yl-4-[4-({[(2,2,4,4-tetrafluoro-4H-1,3-benzodioxin-6-yl)amino]carbonyl}amino)-phenoxy]pyridine-2-carboxamide

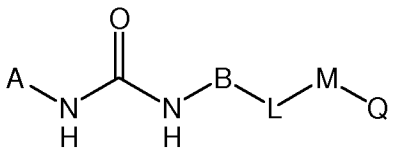
- 4-[4-({[(1-methyl-1H-indazol-5-yl)amino]carbonyl}amino)phenoxy]-N-(2-pyrrolidin-1-ylethyl)pyridine-2-carboxamide
- 4-[4-({[(1-methyl-1H-indazol-5-yl)amino]carbonyl}amino)phenoxy]-N-(2-piperazin-1-ylethyl)pyridine-2-carboxamide
- 4-[2-methoxy-4-({[(2,2,4,4-tetrafluoro-4H-1,3-benzodioxin-6-yl)amino]carbonyl}amino)-phenoxy]pyridine-2-carboxamide
- 4-(4-{[(2,3-dihydro-1H-inden-5-ylamino)carbonyl]amino}-2-methoxyphenoxy)pyridine-2-carboxamide
- 4-[2,5-difluoro-4-({[(2,2,4,4-tetrafluoro-4H-1,3-benzodioxin-6-yl)amino]carbonyl}amino)-phenoxy]pyridine-2-carboxamide
- 4-[3,5-difluoro-4-({[(2,2,4,4-tetrafluoro-4H-1,3-benzodioxin-6-yl)amino]carbonyl}amino)-phenoxy]pyridine-2-carboxamide
- 4-[3-(aminocarbonyl)-4-({[(2,2,4,4-tetrafluoro-4H-1,3-benzodioxin-6-yl)amino]carbonyl}-amino)phenoxy]pyridine-2-carboxamide
- N-methyl-4-[3-(methylsulfonyl)-4-({[(2,2,4,4-tetrafluoro-4H-1,3-benzodioxin-6-yl)amino]carbonyl}amino)phenoxy]pyridine-2-carboxamide
- N-methyl-4-[3-(methylthio)-4-({[(2,2,4,4-tetrafluoro-4H-1,3-benzodioxin-6-yl)amino]carbonyl}amino)phenoxy]pyridine-2-carboxamide
- 4-[3-fluoro-4-({[(6-nitro-1,3-benzothiazol-2-yl)amino]carbonyl}amino)phenoxy]-N-methylpyridine-2-carboxamide
- N-methyl-4-[4-({[(6-nitro-1,3-benzothiazol-2-yl)amino]carbonyl}amino)phenoxy]pyridine-2-carboxamide
- 4-[4-({[(4,6-difluoro-1,3-benzothiazol-2-yl)amino]carbonyl}amino)phenoxy]-N-methylpyridine-2-carboxamide
- N-methyl-4-[4-({[(2-methyl-1,3-benzoxazol-6-yl)amino]carbonyl}amino)phenoxy]pyridine-2-carboxamide
- 4-(4-{[(2,3-dihydro-1H-inden-4-ylamino)carbonyl]amino}phenoxy)-N-methylpyridine-2-carboxamide

- 4-[4-({[(2,2-difluoro-1,3-benzodioxol-4-yl)amino]carbonyl}amino)phenoxy]-N-methylpyridine-2-carboxamide
- N-methyl-4-[4-({[(2-methyl-2H-indazol-5-yl)amino]carbonyl}amino)phenoxy]pyridine-2-carboxamide
- 4-(4-{[({1-[2-(diethylamino)ethyl]-1H-indazol-5-yl}amino)carbonyl]amino}-3-fluorophenoxy)-N-methylpyridine-2-carboxamide
- N-methyl-4-[4-({[(2-methyl-1H-indol-5-yl)amino]carbonyl}amino)phenoxy]pyridine-2-carboxamide
- N-{4-[(2-acetylpyridin-4-yl)oxy]phenyl}-N'-(1-methyl-1H-indazol-5-yl)urea
- N-[2-(dimethylamino)-2-oxoethyl]-4-[4-({[(1-methyl-1H-indazol-5-yl)amino]carbonyl}-aminophenoxy]pyridine-2-carboxamide
- N-methyl-4-[4-({[(2-methyl-1,3-benzothiazol-5-yl)amino]carbonyl}amino)phenoxy]pyridine-2-carboxamide
- N-methyl-4-{[4-({[(1-methyl-1H-indazol-5-yl)amino]carbonyl}amino)phenoxy]methyl}-pyridine-2-carboxamide
- 4-(3-{[(1H-1,2,3-benzotriazol-5-ylamino)carbonyl]amino}phenoxy)-N-methylpyridine-2-carboxamide
- Methyl 4-[3-({[(1-methyl-1H-indazol-5-yl)amino]carbonyl}amino)phenoxy]pyridine-2-carboxylate
- 4-(4-{[(1H-1,2,3-benzotriazol-5-ylamino)carbonyl]amino}phenoxy)-N-methylpyridine-2-carboxamide
- 4-(4-{[(1H-indazol-6-ylamino)carbonyl]amino}phenoxy)-N-methylpyridine-2-carboxamide
- N-methyl-4-{4-[({[2-(trifluoromethyl)-1H-benzimidazol-5-yl]amino}carbonyl)amino]-phenoxy}pyridine-2-carboxamide
- 4-[4-({[(1-ethyl-2-methyl-1H-benzimidazol-5-yl)amino]carbonyl}amino)phenoxy]-N-methylpyridine-2-carboxamide
- Methyl 4-[4-({[(1-methyl-1H-indazol-5-yl)amino]carbonyl}amino)phenoxy]pyridine-2-carboxylate

- 4-[2-chloro-4-({[(2,2,4,4-tetrafluoro-4H-1,3-benzodioxin-7-yl)amino]carbonyl}amino)-phenoxy]-N-methylpyridine-2-carboxamide
- 4-(4-{[(2,3-dihydro-1,4-benzodioxin-6-ylamino)carbonyl]amino}phenoxy)-N-[3-(1H-imidazol-1-yl)propyl]pyridine-2-carboxamide
- 4-(4-{[(2,3-dihydro-1,4-benzodioxin-6-ylamino)carbonyl]amino}phenoxy)-N-(2-pyrrolidin-1-ylethyl)pyridine-2-carboxamide
- N-[3-(1H-imidazol-1-yl)propyl]-4-[4-({[(1-methyl-1H-indazol-5-yl)amino]carbonyl}amino)-phenoxy]pyridine-2-carboxamide
- 4-[4-({[(1-methyl-1H-indazol-5-yl)amino]carbonyl}amino)phenoxy]-N-(2-piperidin-1-ylethyl)pyridine-2-carboxamide
- N-cyclopropyl-4-[4-({[(1-methyl-1H-indazol-5-yl)amino]carbonyl}amino)phenoxy]pyridine-2-carboxamide
- N-(cyclopropylmethyl)-4-[4-({[(1-methyl-1H-indazol-5-yl)amino]carbonyl}amino)phenoxy]-pyridine-2-carboxamide
- N-cyclobutyl-4-[4-({[(1-methyl-1H-indazol-5-yl)amino]carbonyl}amino)phenoxy]pyridine-2-carboxamide or
- Methyl-N-({4-[4-({[(1-methyl-1H-indazol-5-yl)amino]carbonyl}amino)phenoxy]pyridin-2-yl}carbonyl)glycinate.

13) A pharmaceutical composition which comprises an effective amount of at least one compound of claim1 and a physiologically acceptable carrier.

24) A compound of formula (I):

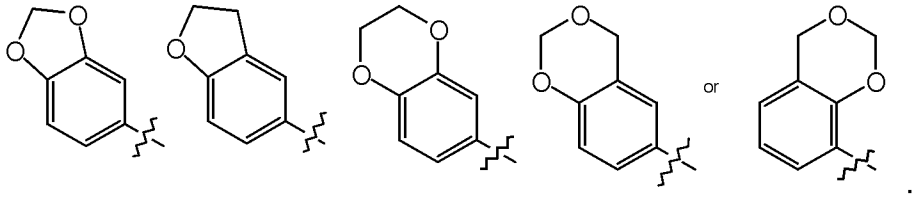


I

wherein
Q is $C(O)R^4$, $C(O)OR^4$ or $C(O)NR^4R^5$;

wherein A is a bicyclic heterocycle which is:

(1) benzimidazol-5-yl
(2) benzimidazol-6-yl
(3) 1,3-benzothiazol-2-yl
(4) 1,3-benzothiazol-5-yl
(5) 1,3-benzothiazol-6-yl
(6) 1,2,3-benzotriazol-5-yl
(7) 1,3-benzoxazol-2-yl
(8) 1,3-benzoxazol-6-yl
(9) 2,3-dihydro-1H-indol-5-yl
(10) 2,3-dihydro-1H-indol-6-yl
(11) 2,3-dihydro-1H-inden-4-yl
(12) 2,3-dihydro-1H-inden-5-yl
(13) 1,1-dioxido-2,3-dihydro-1-benzothien-6-yl
(14) 1H-indazol-5-yl
(15) 2H-indazol-5-yl
(16) 1H-indazol-6-yl
(17) 1H-indol-5-yl
(18) 2-oxo-2H-chromen-7-yl
(19) 1-oxo-2,3-dihydro-1H-inden-5-yl
(20) quinoxalin-2-yl
(21) quinoxalin-6-yl, or
(22) a group of the formula



optionally substituted with 1-4 substituents which are independently R^1, OR^1, $S(O)_pR^1$, $C(O)R^1$, $C(O)OR^1$, $C(O)NR^1R^2$, halogen, oxo, cyano, or nitro

B is phenyl, optionally substituted with 1-4 substituents which are independently C_1-C_5 linear or branched alkyl, C_1-C_5 linear or branched haloalkyl, C_1-C_3 alkoxy, hydroxy, amino, C_1-C_3 alkylamino, C_1-C_6 dialkylamino, carboxyamide, halogen, cyano, nitro or $S(O)_pR^7$;

L is :

(a) $-(CH_2)_m-O-(CH_2)_l-$,
(b) $-(CH_2)_m-(CH_2)_l-$,
(c) $-(CH_2)_m-C(O)-(CH_2)_l-$,
(d) $-(CH_2)_m-NR^3-(CH_2)_l-$,
(e) $-(CH_2)_m- NR^3C(O)-(CH_2)_l-$,
(f) $-(CH_2)_m-S-(CH_2)_l-$,
(g) $-(CH_2)_m-C(O)NR^3-(CH_2)_l-$, or
(h) a single bond;

m and l are integers independently selected from 0-4;

M is a pyridine ring, optionally substituted with 1-3 substituents which are independently C_1-C_5 linear or branched alkyl, C_1-C_5 linear or branched haloalkyl, C_1-C_3 alkoxy, hydroxy, amino, C_1-C_3 alkylamino, C_1-C_6 dialkylamino, halogen, or nitro;

Q is $C(O)R^4$, $C(O)OR^4$ or $C(O)NR^4R^5$;

each of R^1, R^2, R^3, R^4 and R^5, is independently:

(a) hydrogen,
(b) C_1-C_5 linear, branched, or cyclic alkyl,
(c) phenyl,
(d) C_1-C_3 alkyl-phenyl,
(e) up to per–halo substituted C_1-C_5 linear or branched alkyl,
(f) $-(CH_2)_q$-X, wherein X is a 5 or 6 membered heterocyclic ring, containing at least one atom selected from oxygen, nitrogen and sulfur, which is saturated, partially saturated, or aromatic, or a 8-10 membered bicyclic heteroaryl having 1-4 heteroatoms which are O, N or S, or
(g) $-(CH_2)_q$-Y, where Y is $C(O)R^6$, $C(O)OR^6$ and $C(O)NR^6R^7$;

each of R^6 – R^7 is independently :

(a) hydrogen,
(b) C_1-C_5 linear, branched, or cyclic alkyl,
(c) phenyl,
(d) C_1-C_3 alkyl-phenyl, or
(e) up to per–halo substituted C_1-C_5 linear or branched alkyl;

each of R^1, R^2, R^3, R^4, R^5, R^6 and R^7, other than per–halo substituted C_1-C_5 linear or branched alkyl, is optionally substituted with 1-3 substituents which are independently C_1-C_5 linear or branched alkyl, up to perhalo substituted C_1-C_5 linear or branched alkyl, C_1-C_3 alkoxy, hydroxy, carboxy, amino, C_1-C_3 alkylamino, C_1-C_6 dialkylamino, halogen, cyano, or nitro;

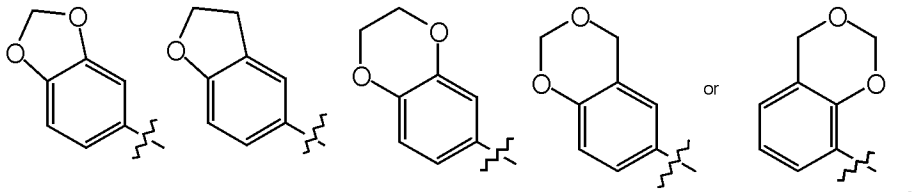
p is an integer selected from 0, 1, or 2; and

q is an integer selected from 1, 2, 3, or 4,

or a pharmaceutically acceptable salt of formula I or an oxidized derivative of formula I wherein one or more urea nitrogens are substituted with a hydroxyl group, or an oxidized derivative of formula I wherein the nitrogen atom of pyridine ring M is in the oxide form, or a methyl, ethyl, propyl, isopropyl, butyl, isobutyl, pentyl ester or phenyl C_1-C_5 alkyl ester of formula I at a carboxylic acid group or amide group.

25) A compound of claim 24 wherein A is selected from

(1) benzimidazol-5-yl
(2) benzimidazol-6-yl
(8) 1,3-benzoxazol-6-yl
(9) 2,3-dihydro-1H-indol-5-yl
(10) 2,3-dihydro-1H-indol-6-yl
(11) 2,3-dihydro-1H-inden-4-yl
(12) 2,3-dihydro-1H-inden-5-yl
(13) 1,1-dioxido-2,3-dihydro-1-benzothien-6-yl
(14) 1H-indazol-5-yl
(15) 2H-indazol-5-yl
(16) 1H-indazol-6-yl
(17) 1H-indol-5-yl
(18) quinoxalin-2-yl
(19) quinoxalin-6-yl, and
(20) a group of the formula



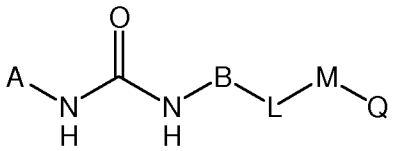
26) A compound of claim 24 wherein the optional substituents on bicyclic heterocycle A are independently R^1, OR^1, and halogen.

27) A compound as in claim 26 wherein B is phenyl optionally substituted with 1-4 substituents which are halogen.

28) A compound of claim 27 wherein L is –O-.

29) A compound of claim 28 wherein Q is $C(O)NR^4R^5$ and each of R^4 and R^5 is independently hydrogen or C_1-C_5 alkyl.

30) A compound of formula (I):



I

wherein

A is a bicyclic heterocycle which is:

(1) benzimidazol-5-yl

(2) benzimidazol-6-yl

(8) 1,3-benzoxazol-6-yl

(9) 2,3-dihydro-1H-indol-5-yl

(10) 2,3-dihydro-1H-indol-6-yl

(11) 2,3-dihydro-1H-inden-4-yl

(12) 2,3-dihydro-1H-inden-5-yl

(13) 1,1-dioxido-2,3-dihydro-1-benzothien-6-yl

(14) 1H-indazol-5-yl

(15) 2H-indazol-5-yl

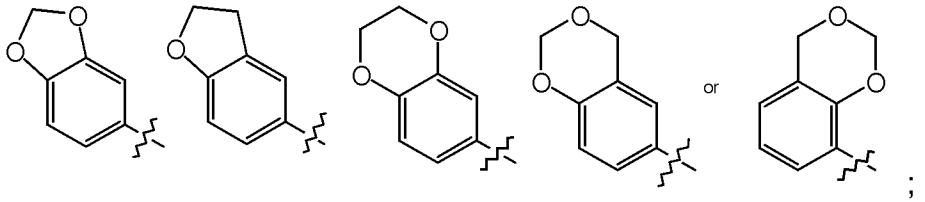
(16) 1H-indazol-6-yl

(17) 1H-indol-5-yl

(18) quinoxalin-2-yl

(19) quinoxalin-6-yl, and

(20) a group of the formula



;

optionally substituted with 1-4 substituents which are independently R^1, OR^1, $S(O)_pR^1$, $C(O)R^1$, $C(O)OR^1$, $C(O)NR^1R^2$, halogen, oxo, cyano, or nitro

B is phenyl, optionally substituted with halogen,

L is -O-,

M is a pyridine ring substituted only with Q,

Q is $C(O)NHR^5$ and R^5 is independently hydrogen or C_1-C_5 alkyl,

and p is an integer selected from 0, 1, or 2

or a pharmaceutically acceptable salt of formula I or an oxidized derivative of formula I wherein one or more urea nitrogens are substituted with a hydroxyl group, or an oxidized derivative of formula I wherein the nitrogen atom of pyridine ring M is in the oxide form, or a methyl, ethyl, propyl, isopropyl, butyl, isobutyl, pentyl ester or phenyl C_1-C_5 alkyl ester of formula I at a carboxylic acid group or amide group.

(ix) EVIDENCE APPENDIX

WO 99/32436

WO 99/32106,

WO 00/55152,

WO 00/55139,

WO 02/83628,

U.S. 6,297,381 and

U.S. 6,525,046.

(x) RELATED PROCEEDINGS APPENDIX

None